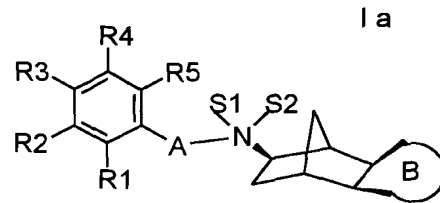
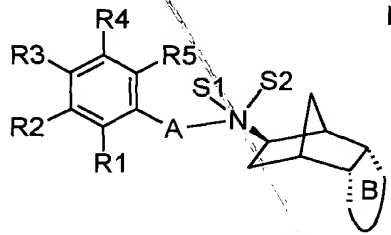


What is claimed is:

1. A substituted norbornylamino derivative having exo-configured nitrogen and an endo-fused five-, six- or seven-membered ring of the formula I or a pharmaceutically acceptable salt or trifluoroacetate thereof, or having exo-configured nitrogen and an exo-fused five-, six- or seven-membered ring of the formula I a or a pharmaceutically acceptable salt or trifluoroacetate thereof



in which:

A is (C<sub>1</sub>-C<sub>4</sub>)-alkylene;

S1 is a free electron pair or (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

S2 is (C<sub>1</sub>-C<sub>4</sub>)-alkyl or H;

where, if S1 and S2 are alkyl, X<sup>-</sup> in the resulting grouping [N<sup>+</sup>(S1S2)-X<sup>-</sup>] corresponds to a pharmacologically acceptable anion or trifluoroacetate;

B is a saturated or unsaturated five-, six- or seven-membered carbon ring which may be mono- or, independently of one another, polysubstituted by oxo, hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxy and (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

and

R1, R2, R3, R4 and R5

are, independently of one another, H, OH, F, Cl, Br, I, CN, NO<sub>2</sub>, amidino, -CO<sub>2</sub>R(11), -CONR(11)R(12), -SO<sub>r</sub>R(11), -SO<sub>s</sub>NR(11)-R(12), (C<sub>1</sub>-C<sub>4</sub>)-alkyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxy, (C<sub>1</sub>-C<sub>4</sub>)-alkoxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyloxy, hydroxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, (C<sub>3</sub>-C<sub>7</sub>)-cycloalkoxy or phenyloxy,

where phenyl is unsubstituted or substituted by up to three substituents, which are independent of one another and are F, Cl, Br, or methoxy;

R1, R2, R3, R4 and R5

or

together are  $-O-CH_2-O-$ :

the remaining radicals R1, R4 and R5

are, independently of one another, H, OH, F, Cl, Br, I, CN, NO<sub>2</sub>, (C<sub>1</sub>-C<sub>2</sub>)-alkoxy, amino, (C<sub>1</sub>-C<sub>2</sub>)-alkylamino or di-(C<sub>1</sub>-C<sub>2</sub>)-alkylamino,

15 where some or all of the hydrogen atoms in the alkyl radicals may be substituted by fluorine;

or a pharmaceutically acceptable salt or trifluoroacetate thereof.

A is (C<sub>1</sub>-C<sub>2</sub>)-alkylene;

S1 is a free electron pair;

25 S2 is H;

**B** is a saturated or unsaturated five- or six-membered carbon ring;

R1, R3 and R5

are hydrogen;

and R2 and R4

30 are, independently of one another, H, methoxy, F or Cl;

or

## R2 and R3

together are  $\text{-O-CH}_2\text{-O-}$ ;

and

35 R1, R4 and R5

are hydrogen;

or a pharmaceutically acceptable salt thereof.

Sub  
pbz

[illegible]

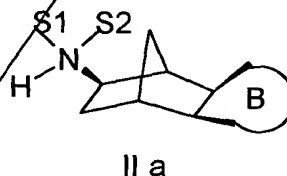
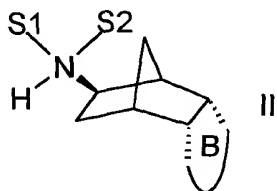
(C) converting the intermediate with suitable reducing agents into a compound of the formula I or Ia, and

(D) optionally converting the compound of the formula I or Ia into a pharmaceutically acceptable salt or trifluoroacetate.

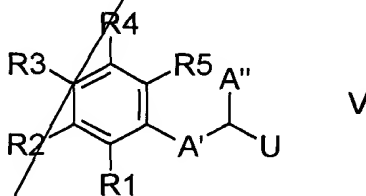
8. A process as claimed in Claim 7, wherein the counterion is chloride or tosylate.

9. A process for preparing a compound of Claim 1, comprising

(A) reacting a compound of the formula II or II a



with an alkylating agent of the formula V



in which U is a nucleophilically substitutable group, and in which S1, S2, B, R1, R2, R3, R4 and R5 are as defined in Claim 1, while independently of one another A' is a bond or (C<sub>1</sub>-C<sub>3</sub>)-alkylene and A'' is H or (C<sub>1</sub>-C<sub>3</sub>)-alkyl and A' and A'' together with the carbon atom to which U is attached represent the same number of carbon atoms as A, to give a compound of the formula I or Ia, and

(B) optionally converting the compound of the formula I or Ia into a pharmaceutically acceptable salt or trifluoroacetate.

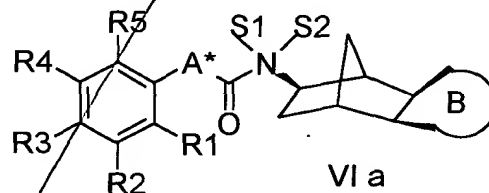
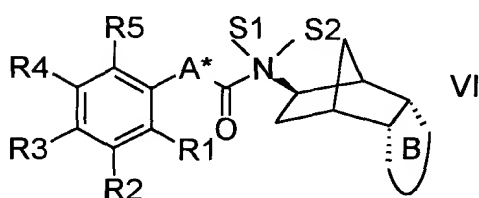
10. A process as claimed in Claim 9, wherein U is chlorine, bromine, iodine, mesylate, tosylate, or triflate.

11. A process as claimed in Claim 9, wherein the reaction step occurs in the presence of one or more non-nucleophilic bases.

12. A process as claimed in Claim 9, wherein the reaction step occurs in the presence of diisopropylethylamine.

13. A process for preparing a compound of Claim 1, comprising

(A) reducing a carboxamide of the formula VI or VI a



in which A\* is a bond or (C<sub>1</sub>-C<sub>3</sub>)-alkylene and the other radicals are as defined in Claim 1 to give a corresponding amine of the formula I or I a, and

(B) optionally converting the amine into a pharmaceutically acceptable salt or trifluoroacetate.

14. A process for converting a secondary amine of the formula I or I a as claimed in claim 1, into a tertiary amine or quaternary ammonium salt, or a pharmaceutically acceptable salt or trifluoroacetate thereof, comprising

(A) mono- or dialkylating a compound of the formula I or Ia in which S1 is a free electron pair and S2 is hydrogen, with alkylating agents of the formula VII



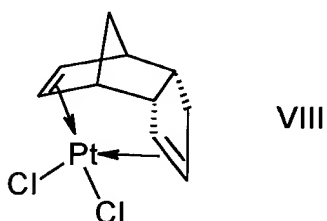
in which S\* is (C<sub>1</sub>-C<sub>4</sub>)-alkyl and U is a nucleophilically substitutable group, thus obtaining a tertiary amine or a quaternary ammonium salt, and

(B) optionally converting the tertiary amine or quaternary ammonium salt into a pharmaceutically acceptable salt or trifluoroacetate.

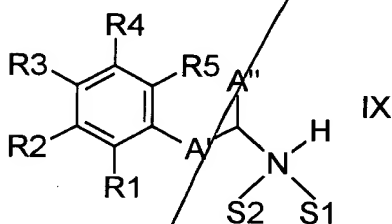
15. A process as claimed in Claim 14, wherein U is chlorine, bromine, iodine, mesylate, tosylate, or triflate.

16. A process for preparing a compound Claim 1, comprising

(A) reacting a dicyclopentadienylplatinum complex of the formula VIII



with amines of the type of the formula IX



in which S1, S2, R1, R2, R3, R4 and R5 are as defined in Claim 1, while independently of one another A' is a bond or (C<sub>1</sub>-C<sub>3</sub>)-alkyl and A'' is H or (C<sub>1</sub>-C<sub>3</sub>)-alkyl and A' and A'' together with the carbon atom to which the nitrogen atom is attached represent the same number of carbon atoms as A, to form an intermediate,

(B) reducing the intermediate formed to give a compound of the formula I, and

(C) optionally converting the compound into a pharmaceutically acceptable salt or trifluoroacetate.

17. A method of treating or preventing one or more disorders of the respiratory drive, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.

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18. A method as claimed in Claim 17, wherein the disorder is sleep-related.

19. A method as claimed in Claim 18, wherein the disorder is sleep apnea.

10 20. A method of treating or preventing snoring, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.

21. A method of treating or preventing one or more acute or chronic renal disorders, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.

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22. A method as claimed in Claim 21, wherein the disorder is acute kidney failure, chronic kidney failure, or both.

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23. A method of treating or preventing impaired intestinal function, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.

24. A method of treating or preventing impaired gallbladder function, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.

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25. A method of treating or preventing ischemic states of the peripheral nervous system, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.

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26. A method of treating or preventing ischemic states of the central nervous system, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.

Sub  
B6  
amt

Sub  
B7  
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Sub  
B8

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35. A composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier.

[illegible]

Sp 25

Sub  
B10

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39. A method of treating or preventing one or more of the following conditions: coronary vasospasms, atherogenesis and atherosclerosis, left-ventricular hypertrophy and dilated cardiomyopathy, and thrombic disorders, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.

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44. A method of treating or preventing organ hypertrophies, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.



Figure 1 is a schematic representation of the experimental design. It shows a sequence of events: Stimulus, Response, Feedback, and Outcome. Arrows indicate the flow from Stimulus to Response, Response to Feedback, and Feedback to Outcome. A Time axis is shown at the bottom, with markers for Stimulus, Response, Feedback, and Outcome.

45. A method of treating or preventing organ hyperplasias, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.
46. A method of treating or preventing a disease caused by elevated cholesterol levels, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.
47. A method of treating or preventing a disease caused by endothelial dysfunction, comprising administering an effective amount of a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof.
48. A method of inhibiting sodium/proton exchanger, subtype 3 (NHE3), in a patient using a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof, comprising giving the patient, for one or more days, up to four doses per day of the compound, wherein the doses are up to 200 mg/kg of body weight.
49. A method of inhibiting sodium/proton exchanger, subtype 3 (NHE3), in a patient using a compound of formula I or I a as claimed in Claim 1 or a pharmaceutically acceptable salt thereof, comprising giving the patient, for one or more days, a daily dose of the compound of between 0.001 mg/kg and 100 mg/kg of body weight.
50. A method as claimed in Claim 49, wherein the daily dose is between 1 and 10 mg/kg of body weight.

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are, independently of one another, H or (C<sub>1</sub>-C<sub>4</sub>)-alkyl,

10

s is 1 or 2;

R1 and R2, R2 and R3, R3 and R4 or R4 and R5

15

and

are, independently of one another, H, OH, F, Cl, Br, I, CN, NO<sub>2</sub>.

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are, independently of one another, H or (C<sub>1</sub>-C<sub>4</sub>)-alkyl,

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s is 1 or 2;

2. A compound of Claim 1, having *exo*-configured nitrogen and an endo-fused five- or six-membered ring of the formula I, or having *exo*-configured nitrogen and an *exo*-fused five- or six-membered ring of the formula I a, in which:

A is (C<sub>1</sub>-C<sub>2</sub>)-alkylene;

[illegible]

5 exo/endo-(3-chlorobenzyl)(octahydro-4,7-methanoinden-5-yl)amine,  
exo/endo-(3-fluorobenzyl)(octahydro-4,7-methanoinden-5-yl)amine,  
exo/endo-benzo[1,3]dioxol-5-ylmethyl(octahydro-4,7-methanoinden-5-yl)-  
amine,  
exo/endo-(*rac*)-(3-methoxybenzyl)(octahydro-4,7-methanoinden-5-yl)-  
10 amine,  
exo/endo-(+)-(3-methoxybenzyl)(octahydro-4,7-methanoinden-5-yl)amine,  
exo/endo-(-)-(3-methoxybenzyl)(octahydro-4,7-methanoinden-5-yl)amine,  
exo/endo-[1-(3-methoxyphenyl)ethyl](octahydro-4,7-methanoinden-5-yl)-  
amine,  
15 exo/endo-(3-fluorobenzyl)(3a,4,5,6,7,7a-hexahydro-1H-4,7-methanoinden-  
5-yl)amine,  
exo/endo-(3-fluorobenzyl)(3a,4,5,6,7,7a-hexahydro-3H-4,7-methanoinden-  
5-yl)amine,  
exo/endo-(3a,4,5,6,7,7a-hexahydro-1H-4,7-methanoinden-5-yl)(3-  
20 methoxybenzyl)amine,  
exo/endo-(3a,4,5,6,7,7a-hexahydro-3H-4,7-methanoinden-5-yl)(3-  
methoxybenzyl)amine,  
exo/endo-(decahydro-1,4-methanonaphthalen-2-yl)(3-methoxybenzyl)-  
amine,  
25 exo/endo-(3,5-difluorobenzyl)(octahydro-4,7-methanoinden-5-yl)amine,  
exo/exo-(3-fluorobenzyl)(octahydro-4,7-methanoinden-5-yl)amine, or  
exo/exo-(3-methoxybenzyl)(octahydro-4,7-methanoinden-5-yl)amine, or  
a pharmaceutically acceptable salt or trifluoroacetate thereof.

30 5. A compound of Claim 1, having exo-configured nitrogen and an endo-fused 5- or 6-membered ring, wherein the compound is:  
exo/endo-(3-chlorobenzyl)(octahydro-4,7-methanoinden-5-yl)amine,  
exo/endo-(3-fluorobenzyl)(octahydro-4,7-methanoinden-5-yl)amine,  
exo/endo-(3-fluorobenzyl)(3a,4,5,6,7,7a-hexahydro-1H-4,7-methanoinden-  
35 5-yl)amine,  
exo/endo-(3-fluorobenzyl)(3a,4,5,6,7,7a-hexahydro-3H-4,7-methanoinden-5-yl)amine,

[illegible]

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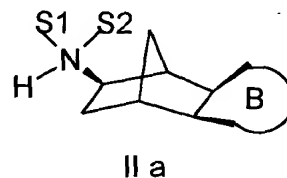
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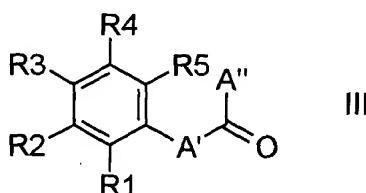
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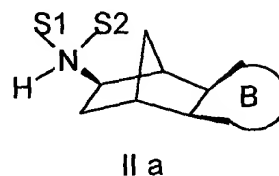
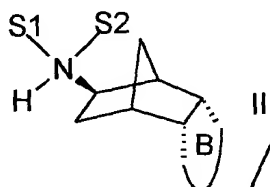
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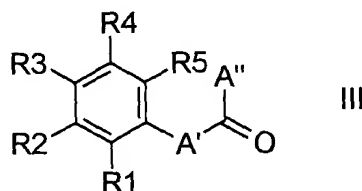
(B) optionally converting the compound of formula I or I a into a pharmaceutically acceptable salt or trifluoroacetate.

7. A process for preparing a compound Claim 1, comprising

(A) reacting a compound of the formula II or II a

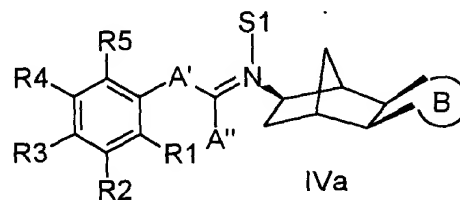
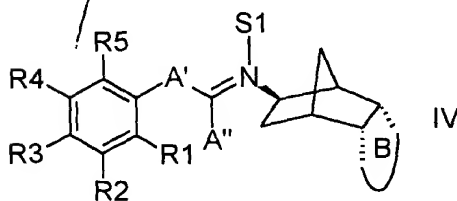


with a compound of the formula III



in which S1, S2, B, R1, R2, R3, R4 and R5 are as defined in Claim 1, while independently of one another A' is a bond or (C<sub>1</sub>-C<sub>3</sub>)-alkylene and A'' is H or (C<sub>1</sub>-C<sub>3</sub>)-alkyl and A' and A'' together with the carbon atom of the carbonyl group represent the same number of carbon atoms as A,

(B) isolating the intermediate of the formula IV or IV a



formed from the reaction of the compounds of the formulae II or II a and III, in which, if S1 is (C<sub>1</sub>-C<sub>4</sub>)-alkyl, an onium nitrogen is formed which is associated with a counterion,